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Persistence of Peak Flow Decrement in Children Following Ozone Exposures Exceeding the National Ambient Air Quality Standard

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P.J. LIOY, T.A. VOLLMUTH, AND M.LIPPMANN

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16. ABSTRACT

Spironmetric measurements of lung function were made on six or more occasions over a five week period in 1982 in 39 children attending a summer day camp in Mendham, N.J. Mean slopes of the linear regressions of FVC, FEV_1, MMEF and PEFR vs. peak 1 hr. O_3 concentrations for the day of the function measurements in the individual children were negative, withPEFR showing the strongest effect. There were no consistent associations with other environmental variables. Analysis of residuals from the regression lines for PEFR vs. daily 1 hr O_3 peak and 4 hr H^+ and $SO_4^=$ exposures for each child showed large overestimates in PEFR during the second week of the study. There was a photochemical smog episode immediately preceding the second week, with successive daily 1 hr O_3 peaks of 143, 185, 165, 135 and 115 ppb, and this smog exposure appears to be the most likely cause of the persistent second week depression in PEFR from the values expected on the basis of an overall regression from the five weeks of data.

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Persistence of Peak Flow Decrement in Children Following Ozone Exposures Exceeding the National Ambient Air Quality Standard

P. J. Lioy, T. A. Vollmuth and M. Lippmann
Institute of Environmental Medicine
New York University Medical Center
Tuxedo, New York

Healthy, active young children in supervised summer recreational programs may be especially sensitive to the effects of ambient ozone (O_3) for several reasons. First, they spend most of their time out of doors during mid-day periods when the outdoor O_3 concentrations are high and indoor concentrations are lower. Second, they engage in vigorous physical activity, which increases their minute ventilation. The activity increases the amount of O_3 inhaled and its penetration into the distal airways where it has its greatest effects on respiratory epithelia. Third, young children are much less likely than adolescents or adults to have had significant exposures to mainstream cigarette smoke or airborne chemicals from occupational or hobby activities. Such exposures could mask or confound the effects of the ambient air pollutant exposures.

We obtained evidence that children's respiratory mechanical function was affected by exposures to ambient O_3 in a two-week pilot study conducted at a summer day camp in Indiana, Pennsylvania in 1980.[1] The highest 1-h O_3 concentration on a study day was 110 ppb by volume, which is below the current National Ambient Air Quality Standard (NAAQS) of 120 ppb. Despite the relatively low ambient air concentrations of O_3, there was evidence of decrements in the forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and peak expiratory flow rate (PEFR). The changes in PEFR were not reported in the paper describing the Indiana study, but were described in our first report of the results of our second summer study by Bock *et al.*[2]

The responses of the children in the first study appeared to be directly related to O_3 exposure, since the potential confounding factors were within ranges that should have severely limited their influence. The ambient temperature was ≤82°F, the 24-h average concentration of total suspended particulate mass (TSP) was ≤66 $\mu g/m^3$, and the 6-h average concentration of sulfuric acid (H_2SO_4) was ≤6 $\mu g/m^3$.

Although the changes in FVC and FEV_1 were small and of uncertain, if any, clinical significance, they were of great interest because they indicated human responses to O_3 at a concentration lower than any previously reported. However, they were consistent with the results of McDonnell *et al.*[3] for clinical tests involving chamber exposures of healthy young nonsmoking adults during vigorous exercise. Small, but statistically significant decrements in symptoms and function were seen at the lowest O_3 concentration used, i.e., 120 ppb.[3]

Although small changes in lung mechanics following individual short-term exposures to O_3 may be of questionable influence on health in themselves, they do indicate that the respiratory tract does respond to low ambient O_3 exposures. The cumulative effects of daily exposures to ambient O_3 are unknown, and need to be defined.

Our main objective in the second summer study was to confirm and extend the relation between O_3 exposure and responses in children. A second objective was to determine, if possible, the influence of other environmental variables, such as temperature and aerosol acidity, on the functional responses to O_3. We elected not to return to Indiana for the second study for several reasons. One was that the camp in Indiana was only operated for two weeks, and we wanted to follow individual children's functions over a longer period of time. Second, we could simplify the logistics of the study, still be in an area subject to ozone episodes, and reduce the costs by selecting a camp within a few hours drive from our laboratory at Tuxedo, New York. The camp which was ultimately selected, with the help of the staff of the Department of Community and Environmental Medicine of the Rutgers Medical School, Piscataway, New Jersey, was located ~3 miles west of Mendham, an upper-middle class suburb on the western edge of the suburban fringe of the New York metropolitan region. It had large grassy fields and a small lake surrounded by woodlands, and was 3.5 miles east of a permanent regional air pollution monitoring station operated by the State of New Jersey at Chester.

As reported by Bock *et al.*[2] we calculated a linear regression between the peak one-hour O_3 concentration for a given day and FVC, FEV_1, PEFR and MMEF as determined for the same day from spirograms for each of the 39 children tested on six or more days. The distribution of the individual slopes for PEFR showed most to be negative. All mean slopes were negative, except for FVC in boys, indicating a general tendency for decreased function with increasing O_3 concentration. In an independent analysis, a summary weighted correlation coefficient between peak O_3 level and each pulmonary function parameter was calculated for each of 49 children seen on four or more days. As in the regression analysis, decrements in PEFR were significantly correlated with the O_3 exposure. Those results are summarized in Table I. In this paper, we extend our past analyses of the spirometric data to examine the persistence of decrements following an elevated period of relatively high O_3 exposure.

Dr. Lioy is presently with the Department of Environmental and Community Medicine, Rutgers Medical School, UMDNJ, Piscataway, NJ 08854. Mr. Vollmuth and Dr. Lippmann are with the Institute of Environmental Medicine, New York University Medical Center, Tuxedo, NY 10987. This note manuscript was peer reviewed.

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Methods

Collection of Health Data

The plan was to enroll all available children ≤13 years of age, and obtain spirometry on as many as possible on each day of the study. This would permit evaluation of exposure-response relationships for each child, and allow the measurements on low exposure days to serve as controls for the child's performance on higher exposure days. During the period from July 12, 1982 to August 12, 1982, measurements were made on 16 camp days. Measurements were not made on rainy days, when the children's activity levels would have been lower, nor on several other days when special camp activities limited our access to the children.

Sixty-two children (25 males, 37 females) between the ages of 7 and 13 years participated in the study. The age and height of each child was recorded upon their entering the study. In addition, a slightly modified standardized questionnaire (ATS-DLD-78C) containing information on each child's history of respiratory illness and household characteristics (i.e., parental occupations, heating and cooking fuel type, family smoking history) was completed by the parent. Although some children were present at camp only during the first two weeks of the study, and others only for the last three weeks, most participated over the five week period.

Spirometry was obtained using an 8-liter survey spirometer equipped with an Eagle I microprocessor (W. E. Collins, Inc., Braintree, Massachusetts) which provided an immediate printout of pre-selected spirometric indices. The calibration of these spirometers was checked daily in the field, and spirometer temperature was recorded prior to testing each child.

On each day of the study, the child performed forced expiratory maneuvers until at least three visually acceptable curves were obtained for which the two largest FVCs differed by no more than 5% as registered on the Eagle I printouts. Spirometric measurements were made only in the afternoon, between approximately 12:00 noon and 3:00 P.M., in order to coincide as much as possible with the expected daily peak in O_3 concentration.

Analysis of Spirometric Data

Each subject's three best spirometric tracings from each test day were analyzed independently by two readers. FVC and FEV_1 were calculated by the backward extrapolation method to determine zero time as recomended by the ATS Snowbird Workshop on Standardization of Spirometry.[4] These values were then compared to those calculated by the Eagle I microprocessor. If they were within 10% of one another, then PEFR, and MMEF (maximum midexpiratory flow rate) i.e., the forced expiratory flow rate between 25% and 75% of FVC, as calculated by the Eagle I, were accepted and recorded for further analysis. If the difference was greater than 10%, then PEFR and MMEF were calculated from the tracing as defined by the ATS Snowbird Workshop and, along with FVC and FEV_1, recorded for later analysis.

Once all the spirometry data were analyzed and filed, they were examined for reader consistency. When there was a 10% or greater discrepancy between the two readers, the tracing was reanalyzed by a third independent reader. The values of FVC and FEV_1 used for subsequent statistical analysis were the maximum taken from any of the acceptable tracings. Values for PEFR and MMEF were taken from the curve with the highest sum of FVC and FEV_1. All volumes were converted to BPTS.

Ambient Air Monitoring and Analysis

Ambient air pollution data were collected nearby in Chester, N.J. at a regional air pollution monitoring station operated by the State of New Jersey Department of Environmental Protection (DEP). Ozone was continuously monitored using a chemiluminescent analyzer (Bendix) and hourly and peak 1-h O_3 concentrations obtained. Since the DEP site was located approximately 3.5 miles west of the daycamp, a second O_3 monitor (Dasibi Environmental Corp.) was operated at the camp. Both instruments were calibrated and quality assured by the DEP. In the field, O_3 levels recorded at both sites correlated well ($r^2 = 0.96$). However, only the O_3 data collected at the DEP site were utilized in the analysis. The O_3 monitor at the camp was inoperative during the first three days of the study, including the day with the highest 1-h ozone concentration, and did not provide a full data set.

At the DEP monitoring site, ambient aerosol samplers were also collected on Teflon filters with a dichotomous sampler having a 15 μm fractionating inlet and a course/fine cut-size of 2.5 μm (Sierra Model 244-E). Two samples were taken daily: one coincided with the pulmonary function testing period (11:30 A.M.–3:30 P.M.); the other during the intermediate time between testing periods. Both fine and coarse filters were extracted in the field in polycarbonate vials containing 10 ml of 1×10^5 M $HClO_4$. These filters were stored in a refrigerator and ultimately sent to and analyzed at EPA's Health Effects Research Lab (HERL) in Research Triangle Park, N.C. Aerosol acidity, as measured by strong acid (H^+) content, was determined using the pH method.[5] Sulfate and nitrate content were measured by ion chromatography.[6]

Ambient temperature, humidity, precipitation and barometric pressure were provided through RSCAN (Dr. W. Lyons, President).[2]

Results

Analyses of Spirometric Measurements

There were 22 girls and 17 boys aged 7–13 who performed acceptable spirometric maneuvers on six or more days during the five week summer camp program. For each child, a linear regression was calculated between the peak hour O_3 concentration for a given day and each of four functional parameters determined for the same day from the spirograms, i.e., FVC, FEV_1, PEFR and MMEF. The regression line slopes were expressed in terms of mL/ppb O_3 for FVC and FEV_1, and mL/s/ppb for PEFR and MMEF. The mean values and standard deviations of the means are summarized in Table I. All mean slopes were negative, except for FVC in boys, indicating a general tendency for decreased function with increasing O_3 concentration. For girls, the decrement in FEV_1, was of borderline significance ($p < 0.10$). The decrement in PEFR was highly significant ($p < 0.005$) for girls and for the population as a whole.

The large variability in the Table I slopes indicated that factors other than the daily peak in O_3 concentration were affecting the pulmonary functions. Preliminary stepwise multiple regression analyses among the significant variables;

Table I. Summary of mean slopes for entire study, July 12 through August 12, 1982. Function change vs. peak ozone concentration.

Group	Number of children	FVC (mL/ppb)	FEV_1 (mL/ppb)	PEFR (mL/s/ppb)	MMEF (mL/s/ppb)
Girls	22	−0.29 ± 1.15	−0.42 ± 1.34	−3.95 ± 4.33	−0.68 ± 2.55
Boys	17	+0.06 ± 1.69	−0.11 ± 1.36	−1.74 ± 5.86	−0.38 ± 3.54
Total	39	−0.12 ± 1.40	−0.28 ± 1.34	−2.99 ± 5.10	−0.55 ± 2.98

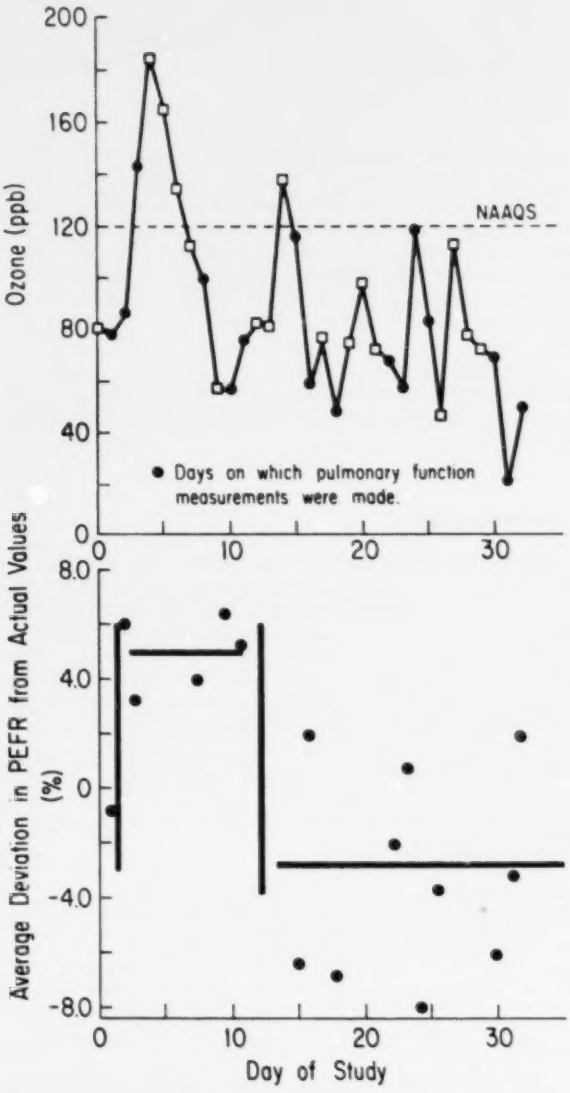
Ozone (ppb)
NAAQS
Days on which pulmonary function measurements were made.
Average Deviation in PEFR from Actual Values (%)
Day of Study

Figure 1. Upper panel: peak one hour ozone concentration vs. day of study in Mendham, N.J. Lower panel: average of the percent deviation of each of the 22 girls' peak expiratory flow rate (PEFR) from PEFR-O_3 regression for that girl vs. day of study. The vertical lines divide the days into those during and the week following the smog episode, and those preceding and following this period. The horizontal lines are the mean values for the separate periods.

date of study, peak ozone, barometric pressure, temperature, sulfate and spirometric temperature, indicated that the number of days from the start of the study was the strongest explanatory variable for pulmonary function variables with a tendency for improved function with increasing day-of-study.

We explored the nature of the day-of-study effect by calculating the average of the deviations (residuals) of the measured function for each child for each day-of-study from the pulmonary function predicted from the O_3 vs. function regression lines. The results are illustrated in Figure 1 for PEFR, with positive values indicating an overprediction by the regression line for the particular day. It can be seen that the average deviation of the measured PEFRs from those predicted were particularly high during the latter part of the first week of the study, and during the second week. The average deviations during the third, fourth and fifth weeks were more randomly distributed around a much lower mean value, and were similar to that seen on the first day of the study.

The remarkably large average deviations in predicted PEFR from the PEFR-O_3 regressions for the second through the 11th day, averaging about +5% as shown in Figure 1, appear to be related to the effects and aftereffects of the prolonged period of high O_3 exposure preceding the second week. The peak 1-hour O_3 concentrations on the five days preceding the second week were 143, 186, 165, 135, and 112 ppb. The period of elevated ozone exposure appeared to have had a cumulative effect on PEFR, producing a shift in the magnitude of the average PEFR residual which persisted for a period which extended at least through the three days when the children were available during the second week. The deviations in MMEF during the second week were of lesser magnitude, but essentially similar in direction and duration. Comparable shifts were not present for either FVC or FEV_1 during the second week.

The accumulation of O_3 during the first week was associated with a large scale regional photochemical smog episode that also produced high concentrations of inhalable particulate matter, including SO_4^{-2}.[7] For the entire five week period, SO_4^{-2} was not related to any overall decrement in pulmonary functions, since the average regression slopes were positive for 22 or more of the 39 children for each function examined. Similarly, there was no apparent effect of H^+ or NO_3^- on function. However, in order to examine whether the H^+, NO_3^-, or SO_4^{-2}, which accumulated during this episode was affecting baseline respiratory function, the day-of-study analysis conducted for O_3 was repeated for H^+, NO_3^-, and SO_4^{-2}. The average deviations of the predicted PEFR on a given day for each pulmonary variable were obtained from the regression equations for each child for the 4-h (11:30 A.M.–3:30 P.M.) H^+, NO_3^-, and SO_4^{-2} concentrations vs. PEFR. The results for H^+ are shown in Figure 2, and indicate a shift in the residual baseline for PEFR, coincident with that associated with O_3. Similar results were also obtained for MMEF as a function variable and for SO_4^{-2} as a pollutant variable. The results for the FVC and FEV_1 regressions with H^+ and SO_4^{-2} differed from the PEFR and MMEF pattern, which was consistent with their lack of an association with O_3 in terms of a persistent response.

Similar analysis of ambient temperature also suggested a day-of-study effect for PEFR. However, the deviations were shifted only for three of the five study days. For NO_3^-, there were no apparent associations.

Since the Mendham study included a photochemical smog pollution episode, the overall results were not directly com-

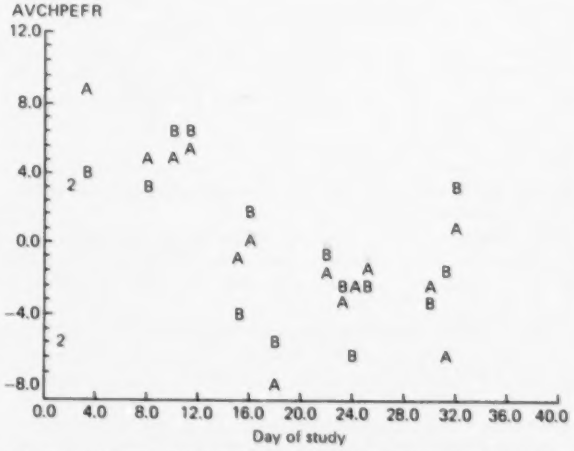

Figure 2. Average of the percent deviation from each child's PEFR from PEFR-pollutant regression for that child vs. day of study. Symbols: A = O_3; B = H^+; 2 = coincident values for O_3 and H^+.

Table II. Summary of mean slopes for period July 26 through August 12, 1983 of function change vs peak ozone concentration.

Group	Number of children	FVC (mL/ppb)	FEV_1 (mL/ppb)	PEFR (mL/s/ppb)	MMEF (mL/s/ppb)
Girls	18	−0.55 ± 2.09	−0.24 ± 1.47	−1.95 ± 4.56[a]	−0.23 ± 2.28
Boys	13	0.36 ± 1.75	0.19 ± 1.90	−1.88 ± 7.33	0.18 ± 2.66
Total	31	−0.17 ± 1.97	−0.06 ± 1.65	−1.92 ± 5.77[a]	−0.06 ± 2.42

[a] $p<0.05$ (one-tailed t-test).

parable to those determined for the Indiana, Pa. study. In an attempt to compare the results from the previous study (which had no smog episode) to those from a corresponding period during the current study, the Mendham data base was truncated to include only the period after the episode when the baseline shift disappeared. The data which remained encompassed the period from July 26 through August 12. The mean PEFR (ml/s/ppb) slopes of the children are shown in Table II. Here again, there was a decrement in PEFR as a function of O_3 concentration. The results were statistically significant ($p \leq 0.05$) for the girls alone and for the entire group of children. For the FVC, FEV_1 and MMEF, the mean slopes were negative for the girls and virtually zero for the boys (Table II). However, none of the slopes were statistically significant. In general, the slopes were not as steep as for the data as a whole, which supports the presence of two effects: one related to the O_3 dose for the day, and the other related to the cumulative effects of a smog episode. The actual cause of the relationship may be much more complicated.

Discussion

The Mendham study regression analyses reported by Bock, *et al.*[2] are generally consistent with those of our earlier study in Indiana, Pa. and those of recent studies of McDonnell, *et al.*,[8] Lebowitz, *et al.*[9] and Linn, *et al.*[10] All report small decrements in one or more respiratory mechanical functions for a short-term exposure among children exposed to O_3 at concentrations ≤150 ppb. The Mendham study analysis of residuals from the regression lines reported in this paper provide evidence for responses of greater potential significance to the future health of the children. They indicate a different kind of response, i.e., a persistent decrement in function lasting for as much as a week after the end of a smog period of about four days duration.

The evidence for a persistent shift of baseline lung function following exposure to a photochemical smog episode presented here does not warrant firm conclusions at this time. Further evidence should be sought in studies involving other children, and a broad range of ambient exposures. However, if several days of ambient smog exposures involving 1-h O_3 concentration peaks in the range of 120–185 ppb consistently produce persistent decrements in lung function in children, then the implications to their health could be serious. The underlying cause of such persistent decrements is not yet known. Some possibilities include altered epithelial permeability and changes in airway secretions. In any case, they represent some response other than the transient changes previously associated with oxidant exposures at and near the current NAAQS.[1,2,8-10]

The extent of the transient responses to O_3 cannot be quantitated accurately when there are persistent responses affecting the same functions. It is likely that the magnitude of the transient PEFR decrement with increasing O_3 concentration is much closer to that shown in Table II than to that in Table I. The slope reported in Table I is greater because it reflects a combination of both the transient and persistent changes caused by the oxidant exposures. In the absence of knowledge of the extent of persistent responses, it is difficult to compare the magnitude of transient effects from different studies.

The transient response appears to be related primarily to O_3, since comparable exposure-response relationships were not seen for the other environmental variables. However, Figure 2 appears to indicate that the persistent effects associated with ozone could have been due to acidic sulfates as well as, or in addition to O_3. Unfortunately, we only collected data for aerosols on the 16 days of function measurements, and do not know the extent of the exposures at the end of the first week. Thus, we still need further studies to clarify the relative roles of O_3 and acid sulfates on respiratory function, and their possible interactions. Such information may be especially important with respect to persistent decrements in function.

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